

By Gerald T. Shekleton
Gerald T. Shekleton
Registration No. 27,466

09/24/98

THE

jc135 U.S. PTO
09/160618
09/24/98

Applicant or Patentee: Edwin H. Christensen

Serial or Patent No.: _____

Filed or Issued: _____

For: SEMI-MOIST ORAL DELIVERY SYSTEM

**VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY
STATUS (37 CFR 1.9(f) and 1.27(b)) - INDEPENDENT INVENTOR**

As a below named inventor, I hereby declare that I qualify as an independent inventor as defined in 37 CFR 1.9(c) for purposes of paying reduced fees under section 41 (a) and (b) of Title 35, United States Code, to the Patent and Trademark Office with regard to the invention entitled SEMI-MOIST ORAL DELIVERY SYSTEM described in

- ☒ the specification filed herewith
☐ application serial no. , filed
☐ patent no. , issued

I have not assigned, granted, conveyed or licensed and am under no obligation under contract or law to assign, grant, convey or license, any rights in the invention to any person who could not be classified as an independent inventor under 37 CFR 1.9(c) if that person had made the invention, or to any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern or organization to which I have assigned, granted, conveyed, or licensed or am under an obligation under contract or law to assign, grant, convey, or license any rights in the invention is listed below:

- ☒ no such person, concern, or organization
☐ persons, concerns or organizations listed below*

*NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

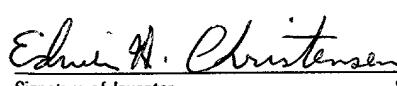
FULL NAME _____
 ADDRESS _____
☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT ORGANIZATION

FULL NAME _____
 ADDRESS _____
☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT ORGANIZATION

FULL NAME _____
 ADDRESS _____
☐ INDIVIDUAL ☐ SMALL BUSINESS CONCERN ☐ NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to pay, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Edwin H. Christensen
 NAME OF INVENTOR NAME OF INVENTOR NAME OF INVENTOR

 Signature of Inventor Signature of Inventor Signature of Inventor

SEPT. 21, 1998
 Date Date Date

09160613 092498
 09160613 092498

73690

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re U.S. Patent Application)
)
Applicant: Edwin H. Christensen)
)
Serial No.: Not Yet Assigned)
)
Filed: September 24, 1998)
)
For: SEMI-MOIST ORAL DELIVERY)
SYSTEM)
)

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This is a Preliminary Amendment for entry in the above-identified application.

In the Specification:

Page 6, line 22 (in the table) delete "17.9" and insert --18.0--.

Page 7, delete the entire line 5 (in the table).

In the Claims:

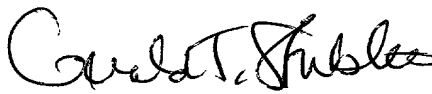
13. The method of claim [10] 12 including adjusting the water content to about 10%.
14. The method of claim [10] 12 including adjusting the polyhydric alcohol content to about 40%.
15. The method of claim [10] 12 including adjusting the starch content to about 32%.
16. The method of claim [10] 12 including adjusting the sugar content to about 15%.
17. The method of claim [10] 12 including adjusting the pregelatinized starch content is about 15%.

05160613-094498
864260-07909760

18. The method of claim [10] 12 including the step of mixing in a pharmaceutical.
19. The method of claim [10] 12 including the step of mixing in a nutraceutical.
20. The method of claim [10] 12 including the step of mixing in a vitamin and mineral mix.
21. The method of claim [10] 12 including the step of adding sorbitol.
22. The method of claim [10] 12 including the step of controlling the A_w to be at about 0.60 to about 0.75.
23. The method of claim [10] 12 including the step of adding aspirin as the active ingredient and controlling the A_w of said carrier to about 0.65.

Respectfully submitted,

WELSH & KATZ, LTD.

By 

Gerald T. Shekleton
Registration No. 27,466

Dated: September 24, 1998

Welsh & Katz, Ltd.
120 South Riverside Plaza
22nd Floor
Chicago, Illinois 60606
Telephone: 312/655-1500



73690

PATENT

I hereby certify that this paper is being deposited with the United States Postal Service as Express Mail in an envelope addressed to: Assistant Commissioner of Patents Washington, D.C., 20231, on this date.

9-24-98 *[Signature]*
Date

Express Mail Label No:

EM443904622US

SEMI-MOIST ORAL DELIVERY SYSTEM

Field of the Invention

This application is directed to a means for delivering pharmaceuticals, nutraceuticals and the like to a mammal and more specifically, the control of the water activity of a food product matrix for use in the incorporation of a pharmaceutical, nutraceutical or other bioactive compound into the matrix.

Background of the Invention

Pharmaceutical and nutraceutical products intended for oral administration are typically provided in tablet, capsule, pill, lozenges and caplet form. These products are swallowed whole or chewed in the mouth for delivery of the active ingredient into the alimentary system of a body. Such oral delivery systems are sometimes made chewable to ease drug administration in pediatric and geriatric patients. Such concerns with ease of administration may be amplified when dealing with pets and other animals.

As a result, several approaches have been utilized in formulating oral delivery systems, including gums and candy bases. The use of such delivery systems is limited by the

reaction of the active ingredient, whether it be pharmaceutical, nutraceutical or other ingredients, to the existence of water in the system.

Summary of the Invention

Therefore, an object of the subject invention is a method of controlling water activity in an oral delivery system and the product thereof.

A further object of the subject invention is a oral delivery system for pharmaceuticals, nutraceuticals or other active ingredient which matches the water activity of the carrier to the included active ingredient.

Description of the Preferred Embodiments

By the subject invention, a soft chewable oral delivery system is provided. The dosage form may be in tablet form and may contain one or more active ingredients. The active ingredients are incorporated into the system which is described in further detail below and which includes a starch component, a fat or oil, a sugar component, a polyhydric alcohol, water and other minor ingredients. Into this mixture is placed the active ingredient. After mixing and extruding these ingredients, the extrudate is formed into the appropriate shape. The relative proportions of the mixture are as follows.

Starch	10-50%
Fat or Oil	0-40%
Sugar	5-25%
Polyhydric Alcohol	10-50%

but are not limited to ethylene oxide, propylene oxide, acetic anhydride, and succinic anhydride, and other food approved esters or ethers, introducing such chemicals alone or in combination with one another. Prior crosslinking of the starch may or may not be necessary based on the pH of the system and the temperature used to form the product.

5 By "amylaceous ingredients" is meant those food-stuffs containing a preponderance of starch and/or starch-like material. Examples of amylaceous ingredients are cereal grains and meals or flours obtained upon grinding cereal grains such as corn, oats, wheat, milo, barley, rice, and the various milling by-products of these cereal grains such as wheat feed flour, wheat middlings, mixed feed, wheat shorts, wheat red dog, oat groats, hominy feed, and other such material. Also included as sources of amylaceous ingredients are the tuberous food stuffs such as potatoes, tapioca, and the like.

Another component of the matrix is a fat component such as fat or oil of animal or vegetable origin. Typical animal fats or oils are fish oil, chicken fat, tallow, choice white grease, prime steam lard and mixtures thereof. Other animal fats are also suitable for use in the matrix. Vegetable fats or oils are derived from corn, soy, cottonseed, peanut, flax, rapeseed, sunflower, other oil bearing vegetable seeds, and mixtures thereof. Additionally, a mixture of animal or vegetable oils or fats is suitable for use in the matrix. The fat component of the matrix is about 0 to about 40 % by weight of the matrix. More specifically, the fat component of the matrix is about 20 percent by weight of the matrix.

20 The polyhydric alcohol component of the matrix can be selected from glycerol, sorbitol, propylene glycol, 1,3-butanediol, and mixtures thereof with each other and other polyhydric alcohols. Generally the polyhydric alcohol comprises about 10 to about 50 percent

by weight of the matrix. More specifically, the polyhydric alcohol comprises about 20 to about 40 percent by weight of the matrix.

The sugar component can be employed in a dry or crystalline condition or can be an aqueous syrup having a sugar concentration of from 50 to about 95, preferably from 70 to about 80, weight percent. The sugar used can be lactose, sucrose, fructose, glucose, or maltose, depending on the particular application and price or availability of a particular sugar. Examples of various well established sources of these sugars are, corn syrup solids, malt syrup, hydrolyzed corn starch, hydrol (syrup from glucose manufacturing operations), raw and refined cane and beet sugars, etc.

Water must be present in the matrix at least about 5 percent by weight of the matrix. More specifically, water is present in the matrix about 5 percent to about 20 percent by weight of the matrix. The matrix thus formed usually has a water activity of 0.60 to 0.75.

While water must be at least 5 percent by weight of the matrix, when the matrix is used in a food product, the moisture of the food product must be adjusted. Generally the moisture content of the matrix is such to give a moisture content of 5-15 percent to the final soft dry food product. More preferred is a moisture content of 5 percent to 14 percent. Most preferred is a moisture content of 8 percent to 13 percent. The desired moisture content may be achieved in any suitable fashion. Normal processing may produce the moisture content desired. A standard drying step is optional and may be used if necessary.

The active ingredient may be any drug, nutrition agent, or the like which can be orally administered. Exemplary of such active ingredients are the following: nutraceuticals, such as chromium picolinate, potassium gluconate and methionine amino acid; prescription drugs,

such as ivermectin, fenbendazole, piperazine, magnesium hydroxide, stranzole, furosemide, penicillin, amoxicillin, prednisolone, methylprednisolone, acepromazine; and, other pharmaceutical products, such as aspirin, prozac, zantac, and benedryl. Minor amounts of flavorants, colorants, glycerin, flavor enhancers, sweeteners, emulsifiers, antibitterness agents, taste masking agents, stabilizers, preservatives, or combinations thereof may be added.

To form the matrix, the starch system, fat, polyhydric alcohol, corn syrup and water are mixed with a screw extruder, permitting addition of ingredients and variable heating at different points along the barrel. Other mixing apparatus, such as a sigma mixer, swept wall heat exchanger or the like may be used. If a coloration is desired in the final product, cooked or pregelled starches are used to form the matrix. The use of these starches avoids high cooking temperatures which would destroy the desire coloration and/or active ingredient. If coloration active temperature sensitivity is not a problem, it is possible to use an uncooked or ungelatinized starch to form the matrix and cook or gel the starch as the process is carried out. The incorporation of a derivatized starch in the product more clearly guarantees the softness of the product for a longer period of time. Softness is also provided by the fats and oils. In this fashion a suitable matrix is provided for use with a wide variety of active ingredients.

Having fully described the invention, the following examples are presented to illustrate the invention without limitation thereof. In these examples all parts percentages are by weight unless otherwise specified.

EXAMPLE 1 -- Carrier

INGREDIENT	PARTS
Regular Corn Starch (Purefood GMI)	17.9

Pregel Starch (SOFT SET)	15.0
Corn Syrup (Star Dri Corn Syrup Solids)	15.0
Corn Oil	20.0
Sorbitol	20.0
Active	0.1
H ₂ O	10.0
Salt	2.0
TOTAL	100.0

The above ingredients are mixed at temperatures of about 125°F, extruded and cut into a suitable tablet size. This product has an oily, bubbly appearance suggesting cutting back on the oil content. Temperature was also adjusted during each of the following examples to eliminate puffing of the product as it exits the extruder.

EXAMPLE 2 -- Guaifenesin

INGREDIENT	PARTS
Regular Corn Starch (Purefood GMI)	17.9
Pregel Starch (SOFT SET)	15.0
Corn Syrup (Star Dri Corn Syrup Solids)	15.0
Sorbitol	39.3
H ₂ O	10.0
Salt	2.0
Guaifenesin*	0.8
TOTAL	100.0

* Available from Arrow Chemical Co., N.J.

EXAMPLE 3 -- Vitamins

INGREDIENT	PARTS
Regular Corn Starch (Purefood GMI)	17.9
Pregel Starch (SOFT SET)	15.0
Corn Syrup (Star Dri Corn Syrup Solids)	15.0
Sorbitol	35.1
H ₂ O	10.0
Salt	2.0
Vitamin and Mineral Mix*	5.0
TOTAL	100.0

* Commercially available mixture available from Archer Daniels Midland.

EXAMPLE 4 -- Flax

INGREDIENT	PARTS
Regular Corn Starch (Purefood GMI)	17.9
Pregel Starch (SOFT SET)	15.0
Corn Syrup (Star Dri Corn Syrup Solids)	15.0
Sorbitol	35.1
H ₂ O	10.0
Salt	2.0
Flax*	5.0
TOTAL	100.0

*Available from Enreco Flax.

EXAMPLE 5 -- Acetaminophen

INGREDIENT	PERCENT
Regular Corn Starch (Purefood GMI)	17.9
Pregel Starch (SOFT SET)	15.0
Corn Syrup (Star Dri Corn Syrup Solids)	15.0
Sorbitol	39.1
H ₂ O	10.0
Salt	2.0
Acetaminophen*	0.8
Red Coloring #40	0.1
Flavoring (Cherry)	0.1
TOTAL	100.0

* Available from Mallinckrodt as Compap

EXAMPLE 6 -- Carrier

INGREDIENT	PARTS
Regular Corn Starch (Purefood GMI)	17.9
Pregel Starch (SOFT SET)	15.0
Corn Syrup (Star Dri Corn Syrup Solids)	15.0
Sorbitol	40.1
H ₂ O	10.0
Salt	2.0
TOTAL	100.0

TABLE 1

Example	Active	Oil/Sugar	A _w	Extrusion Temp.
1	Premix	Corn Oil/Sorbitol	N/A	125
2	Guaifenesin	100% Sorbitol	0.656	115
3	Vitamin Mix	100% Sorbitol	0.651	115
4	Flax	100% Sorbitol	0.673	115
5	Acetaminophen	100% Sorbitol	0.666	115
6	Premix	100% Sorbitol	0.61	115

By the above examples and Table 1 it is apparent that an oral delivery system for the administration for pharmaceuticals, nutraceuticals, vitamins and minerals and other active ingredients may be provided in a chewable form by the subject invention. If the active ingredient is water sensitive such as aspirin, then the amount of polyhydric alcohol is increased, the water activity is depressed to about 0.65 and the stability and texture of the resultant product is maintained. If the active ingredient requires or can tolerate the presence of free water for its activity, such as in the case of Guaifenesin, the amount of polyhydric alcohol may be decreased, while maintaining the level of such polyhydric alcohol such that a soft texture of the resulting tablet is maintained. In the case of Guaifenesin, then an A_w of 0.70 may be utilized and a softer, more chewable texture achieved. An effective oral delivery system in which the texture and stability of the product and activity of the active ingredient is controllable, is the result.

5

Various features of the invention are set forth in the following claims.

What is claimed is:

1. A carrier for the oral administration of an active ingredient to mammals comprising:

10-50% starch,

0-40% fat or oil,

8-50% polyhydric alcohol,

5-25% sugar

5-20% water, and

1-5% salt

said carrier having an A_w of about 0.60 to 0.75.

2. The carrier of claim 1 wherein the water content is about 10%.
3. The carrier of claim 1 wherein the polyhydric alcohol content is about 40%.
4. The carrier of claim 1 wherein the starch content is about 32%.
5. The carrier of claim 1 wherein the pregelatinized starch content is about 15%.
6. The carrier of claim 1 wherein the active ingredient is a pharmaceutical.
7. The carrier of claim 1 wherein the active ingredient is a nutraceutical.

8. The carrier of claim 1 wherein the active ingredient is a vitamin and mineral mix.
9. The carrier of claim 1 where the A_w is 0.65 and the active ingredient is aspirin.
10. The carrier of claim 1 wherein the polyhydric alcohol is sorbitol.
11. The carrier of claim 1 wherein the sugar content is about 15%.
12. A method of making a carrier for an active ingredient for use in an oral administration of the active ingredient, comprising the steps of:
 - a) forming a matrix by mixing
 - 10-50% starch,
 - 0-40% fat or oil,
 - 10-50% polyhydric alcohol,
 - 5-25% sugar,
 - 5-20% water, and
 - 1-5% salt
 - b) adjusting the relative amounts of polyhydric alcohol and water to control the A_w of said carrier;

whereby the controlled A_w permits the moisture in the carrier to be at a level not inimical to the active ingredient.

13. The method of claim 10 including adjusting the water content to about 10%.
14. The method of claim 10 including adjusting the polyhydric alcohol content to about 40%.
15. The method of claim 10 including adjusting the starch content to about 32%.
16. The method of claim 10 including adjusting the sugar content to about 15%.
17. The method of claim 10 including adjusting the pregelatinized starch content is about 15%.
18. The method of claim 10 including the step of mixing in a pharmaceutical.
19. The method of claim 10 including the step of mixing in a nutraceutical.
20. The method of claim 10 including the step of mixing in a vitamin and mineral mix.
21. The method of claim 10 including the step of adding sorbitol.

22. The method of claim 10 including the step of controlling the A_w to be at about 0.60 to about 0.75.

23. The method of claim 10 including the step of adding aspirin as the active ingredient and controlling the A_w of said carrier to about 0.65.

09460613.0249
064260" 87305760

ABSTRACT

These and other objects are attained by the subject invention wherein there is provided a carrier or product formed of a matrix having starch, sugar, fat, polyhydric alcohol and water in suitable ratios such that there exists a water activity of 0.6-0.75. The water activity of the product matrix is adjusted up or down so that the availability of water in the finished product is not detrimental to the included active ingredient, be it pharmaceutical, nutraceutical, or a vitamin mineral complex.

03460648-034498

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare:

That my residence, post office address and citizenship are as stated below next to my name.

That I verily believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **SEMI-MOIST ORAL DELIVERY SYSTEM** the specification of which (check one)

☒ is attached hereto.

☐ was filed on _____ as Application, Serial No. _____ and was amended on _____ (if applicable).

That I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

That I acknowledge the duty to disclose information known to be material to patentability of this application in accordance with Title 37, Code of Federal Regulations §1.56(a).

That I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate on this invention having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)

Priority Claimed

(Number) (Country) (Day/Month/Year Filed)

☐ ☐
Yes No

(Number) (Country) (Day/Month/Year Filed)

☐ ☐
Yes No

That I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

United States Application(s)

(Application Serial No.) (Filing Date) (Status)-(Patented, pending, abandoned)

(Application Serial No.) (Filing Date) (Status)-(Patented, pending, abandoned)

09360618 064260" ST909T60

That all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

I hereby appoint the following attorneys, with full power of substitution and revocation, to prosecute this application and to transact all business in the United States Patent and Trademark Office connected therewith and request that all correspondence and telephone calls in respect to this application be directed to: WELSH & KATZ, LTD., 120 South Riverside Plaza, 22nd Floor, Chicago, Illinois 60606-3913, Telephone No.: (312) 655-1500:

<u>Attorney</u>	<u>Registration No.</u>
Donald L. Welsh	16,665
A. Sidney Katz	24,003
Richard L. Wood	22,839
Jerold B. Schnayer	28,903
Eric C. Cohen	27,429
Joseph R. Marcus	25,060
Gerald S. Schur	22,053
Gerald T. Shekleton	27,466
James A. Scheer	29,434
Daniel R. Cherry	29,054
Edward P. Gamson	29,381
Kathleen A. Rheintgen	34,044
Thomas W. Tolpin	27,600

Full name of sole or one
joint inventor:

Edwin H. Christensen

Inventor's signature:

Edwin H. Christensen

Date:

SEPT. 21, 1958

Residence and Post Office Address:

5022 N.W. 104th Way

Coral Springs, Florida 33076

Citizenship:

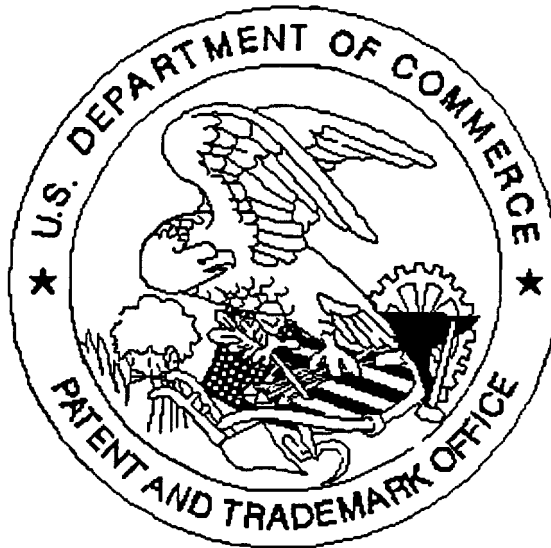
U.S.A.

Address for Correspondence:

WELSH & KATZ, LTD.
120 South Riverside Plaza
22nd Floor
Chicago, Illinois 60606-3913

United States Patent & Trademark Office

Office of Initial Patent Examination -- Scanning Division



Application deficiencies found during scanning:

1. Application papers are not suitable for scanning and are not in compliance with 37 CFR 1.52 because:
 - ☐ All sheets must be the same size and either A4 (21 cm x 29.7 cm) or 8-1/2"x 11"
Pages _____ do not meet these requirements.
 - ☐ Papers are not flexible, strong, smooth, non-shiny, durable, and white.
 - ☐ Papers are not typewritten or mechanically printed in permanent ink on one side.
 - ☐ Papers contain improper margins. Each sheet must have a left margin of at least 2.5 cm (1") and top, bottom and right margins of at least 2.0 cm (3/4").
 - ☐ Papers contain hand lettering.
2. Drawings are not in compliance and were not scanned because:
 - ☐ The drawings or copy of drawings are not suitable for electronic reproduction.
 - ☐ All drawings sheets are not the same size. Pages must be either A4 (21 cm x 29.7 cm) or 8-1/2" x 11".
 - ☐ Each sheet must include a top and left margin of at least 2.5 cm (1"), a right margin of at least 1.5 cm (9/16") and a bottom margin of at least 1.0 cm (3/8").
3. Page(s) _____ are not of sufficient clarity, contrast and quality for electronic reproduction.
4. Page(s) _____ are missing.
5. OTHER: NO DRAWINGS